

### REMARKS

Claims 1-12, 25-28, and 30-38 are pending by way of the present amendment, claims 1, 4, and 5 having been amended and claims 31-38 added. Withdrawn claims 14-24 and 29 are canceled by this amendment.

#### Information Disclosure Statement

The Examiner indicated that Reference JP 05-328969 was not considered because a copy was not submitted with a previously filed Information Disclosure Statement. Submitted herewith is an Information Disclosure Statement including the reference indicated by the Examiner. Accordingly, the matter regarding an Information Disclosure Statement is resolved.

#### Objections to Specification

The specification was objected to as containing informalities requiring correction. The typographical error "resent" was replaced with "recent." In this amended paragraph, it is to be understood that the terms "Thermus aquaticus" and "Thermus thermophilus" were underlined in the original specification and are not meant to indicate amendments.

The location of the description of the figures near the end of the specification was objected to. In response, the description of the figures was moved forward in the specification.

Clarification was requested regarding "Reference Example 1" and "Example 1." In response, the specification was amended to clarify the distinction between "Reference Example 1" and "Example 1."

The specification was objected to as not in compliance with 37 C.F.R. 1.821-1.825 regarding sequence disclosures. Submitted herewith is a supplemental Sequence Listing, a computer readable copy, and a Statement in accordance with 37 C.F.R. 1.821-1.825. The supplemental Sequence Listing contains six sequences, SEQ ID NOS 29-34, as suggested by the Examiner. Accordingly, the objections to the specification are overcome.

### Objections to Claims

Claim 1 was objected to as containing informalities requiring correction. The objected-to language "the EXO I region" was replaced with "the exonuclease I region." Accordingly, the objections to the claims are overcome.

### 112, 2<sup>nd</sup> paragraph. Rejections to Claims

Claims 1-12, 25-28, and 30 were rejected as being indefinite. In particular, claim 1 was rejected as being indefinite in that language used was considered repetitive and unclear. Claims 4 and 5 were rejected as being indefinite for having insufficient antecedent basis. The objected-to language of claims 1, 4, and 5 was amended as suggested by the Examiner. The rejections are therefore overcome.

### 112, 1<sup>st</sup> paragraph. Rejections of Claims

Claims 1-3, 25-28, and 30 were rejected as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. The Examiner also alleged that the specification did not support the scope of the claims which encompassed all modification and fragments of modified thermostable DNA polymerase. See the Office Action, pages 9-10. Applicants respectfully disagree.

It is known that the exonuclease I region of the thermostable DNA polymerase is highly conserved. For example, the  $X_0DX_1EX_2$  sequence in the EXO I region is conserved in archaeon- and phage-derived DNA polymerases (see Fig. 1, for example).

However, as shown in Fig. 1, the  $DX_1EX_2X_3X_4H$  sequence is not always conserved, especially "H". More specifically, in Fig. 1, KOD(Pyrococcus), Pfu(Pyrococcus) and Vent(Thermococcus) have the  $DX_1EX_2X_3X_4H$  sequence, but Sso(Sulfolobus; DIEVYTP) does not have the  $DX_1EX_2X_3X_4H$  sequence. Phage-derived DNA polymerases do not have the  $DX_1EX_2X_3X_4H$  sequence, either.

Embodiments of the present invention are directed to specific DNA polymerases having the  $DX_1EX_2X_3X_4H$  sequence. As to DNA polymerases having the  $DX_1EX_2X_3X_4H$  sequence, it is fully supported that replacement of histidine(H) by another amino acid, especially an amino acid

selected from the group consisting of aspartic acid, glutamic acid, tyrosine, alanine, lysine and arginine (claim 2) results in modified thermostable DNA polymerase with:

- (i) significantly reduced 3'-5' exonuclease activity;
- (ii) improved amplifying efficiency; or
- (iii) significantly improved 3'-5' exonuclease activity and/or fidelity on a DNA replication or amplification.

Accordingly, Applicants respectfully submit that the specification provides adequate written description and enablement of the claims as currently amended. Thus, Applicants respectfully request that the rejections be withdrawn.

### CONCLUSION

The claims are believed to be in condition for allowance and an early and favorable action to that effect is requested.

The Examiner is invited to contact the undersigned at 202-220-4200 to discuss any matters regarding this application.

The Office is authorized to charge the fee for a Petition for an Extension of time and any other fees under 37 C.F.R. 1.16 and 1.17 and credit any overpayment to Kenyon & Kenyon Deposit Account No. 11-0600.

Respectfully submitted,  
KENYON & KENYON

Date:

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W. David Wallace  
Reg. No. 42,210

1500 K Street, NW - Suite 700  
Washington, DC 20005  
telephone: 202-220-4200  
facsimile: 202-220-4201

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